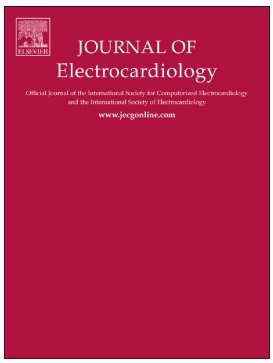


Non-invasive electrophysiological assessment of the optimal configuration of quadripolar lead vectors on ventricular activation times

Helder Pereira, Tom A. Jackson, Benjamin Sieniewicz, Justin Gould, Cheng Yao, Steven Niederer, Christopher A. Rinaldi

PII: S0022-0736(18)30176-6
DOI: doi:10.1016/j.jelectrocard.2018.05.006
Reference: YJELC 52625

To appear in:

Please cite this article as: Helder Pereira, Tom A. Jackson, Benjamin Sieniewicz, Justin Gould, Cheng Yao, Steven Niederer, Christopher A. Rinaldi , Non-invasive electrophysiological assessment of the optimal configuration of quadripolar lead vectors on ventricular activation times. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Yjelc(2017), doi:10.1016/j.jelectrocard.2018.05.006

Non-invasive electrophysiological assessment of the optimal configuration of quadripolar lead vectors on ventricular activation times

Helder Pereira, MSc,[a] Tom A. Jackson, MBBS,[ab] Benjamin Sieniewicz, MBChB,[ab] Justin Gould, MBBS,[ab] Cheng Yao, PhD,[c] Steven Niederer, DPhil,[a] and Christopher A. Rinaldi, MD[ab]

[a] Division of Imaging Sciences and Biomedical Engineering, King's College London, London, United Kingdom, [b] Cardiovascular Department, Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom, and [c] Medtronic Ltd, United Kingdom

Address for reprint requests and correspondence: Helder Pereira, Division of Imaging Sciences and Biomedical Engineering, King's College London, 4th Floor, Lambeth Wing, St. Thomas' Hospital, Westminster Bridge Rd, London SE1 7EH, United Kingdom. E-mail address: helder.pereira@kcl.ac.uk

Structured abstract

Background: Cardiac resynchronization therapy (CRT) is now generally delivered via quadripolar leads. Assessment of the effect of different vector programs from quadripolar leads on ventricular activation can be now done using non-invasive electrocardiographic mapping (ECM).

Material and methods: In nineteen patients with quadripolar LV leads, activation maps were constructed. The total ventricular activation time (TVaT) and the time for the bulk of ventricular activation (VaT_{10-90}) were calculated.

Results: CRT delivered via a quadripolar lead significantly reduced TVaT and VaT_{10-90} by a mean of 16ms and 31ms, respectively, compared to baseline. There was a marked reduction in

ventricular activation between the most and least synchronous vectors: 28% difference in baseline TVaT and 37% difference in VaT_{10-90}.

Conclusion: Changes in the configuration of an LV quadripolar lead significantly affected ventricular activation timings in both ischaemic and non-ischaemic subjects. This suggests that programming of the optimal pacing vector may need to be individually tailored.

Keywords

Cardiac resynchronization therapy; Non-invasive electrocardiographic mapping; quadripolar left ventricular lead; Optimisation; Ventricular activation time;

Introduction

Cardiac resynchronisation therapy (CRT) is an effective treatment for patients with heart failure and electrical dyssynchrony[1] and is now generally delivered via quadripolar leads that allow stimulation via multiple pacing vectors.[2] This may permit more basal activation of the LV, which may improve resynchronisation and avoid areas of scar or phrenic nerve stimulation (PNS), which are both associated with a reduced response to CRT.[3] Quadripolar leads improve morbidity and mortality and also offer economic benefits over bipolar leads.[4,5] Although quadripolar leads provide multiple vector options, there is no indication that a particular vector delivers the best result, nor if a selected vector offers better or worst effects to a specific group of patients. Selection and programming of the optimal vector with quadripolar leads may be patient specific. The presence of scar and pattern of dyssynchrony may limit effective myocardial stimulation that may be overcome by optimising the LV vector to improve electrical resynchronisation. As such there may be differences between ischemic and non-ischaemic patients. We have previously shown that changes in invasively measured total ventricular activation time (TVaT) and the time for the 10^{th} to 90^{th} percentiles of the myocardium to activate (VaT_{10-90}) reflecting the bulk of myocardial activation predict CRT response.[6] Electrocardiographic mapping (ECM) is a non-invasive mapping technique that provides detailed patient-specific information on epicardial electrical activation enabling the measurement of activation times from the epicardium of the LV and right ventricle (RV) non-invasively with different quadripolar configurations.[7,8]

We hypothesised that stimulation from different vectors of a quadripolar lead would have different effects on left ventricular activation times, which may be important in determining the optimal programming. To assess this, we used ECM to investigate the associations between various LV-stimulation configurations with a quadripolar LV lead by measuring the respective total activation times of the ventricles with regard to the subject characteristics with a focus on the underlying aetiology.

Material and methods

This was a prospective single-site study of progressive heart failure (HF) patients receiving CRT. The study conformed to the principles outlined in the Declaration of Helsinki on research in human subjects. All subjects gave their written informed consent to participate in the study (approved by the Research Ethics Committee, ClinicalTrials.gov Identifier: NCT01831518.). All subjects fulfilled criteria for CRT implantation: NYHA Class II-IV; echocardiographic Left Ventricular Ejection Fraction (LVEF) < 35%, QRS duration > 120 ms (independently of the QRS morphology) and optimal medical therapy (OMT) for heart failure. The aetiology of heart failure was classified as ischaemic in the presence of substantial coronary artery disease or a history of myocardial infarction or revascularisation, and as non-ischaemic otherwise. Intraventricular conduction disturbances were defined according to the AHA/ACCF/HRS Recommendations for the Standardization and Interpretation of the Electrocardiogram.[9] 12-lead ECGs were acquired with a GE Mac 5000 ECG system (General Electric-Vingmed, Milwaukee, WI) using standard American Heart Association (AHA)-recommended filter settings [10] at a sweep rate of 25 mm/s and a gain of 10 mm/mV. Echocardiography was performed using an IE33 or EPIC model scanner (Philips Healthcare, Best, The Netherlands).

CRT implantation

Implantation was performed via the cephalic and/or axillary veins with the RV lead implanted at the RV apex or high septum at the discretion of the implanting physician, and the right atrial lead placed at the right atrial appendage. All patients were implanted with a St. Jude Medical Quartet lead™, which offers 10 different LV configurations through its quadripolar electrodes – this lead was preferentially sited in the lateral or postero-lateral vein tributary of the coronary sinus. The operator sought to have all four poles of the quadripolar lead within the vein to allow for stimulation from all the poles. If this was not possible due to technical difficulties or because of unacceptable pacing thresholds or PNS, an alternative location was chosen in the anterolateral,

posterior, or anterior locations. Following implantation, posteroanterior and lateral chest radiographic images were obtained according to standard protocols.

Electrocardiographic mapping

Echo-guided optimisation was performed the day following implantation: AV intervals through the Iterative method [11] and VV intervals by assessment of the left ventricular outflow tract velocity time integral (LVOT VTI) [12]. Participants underwent ECM using a CardioInsight ECVUE system (CardioInsight Technologies Inc., Cleveland, OH) to non-invasively provide biventricular epicardial ventricular electrograms and construct 3D isochrone and isopotential activation maps.[13] ECM maps were created on a beat-by-beat basis for all the available quadripolar LV lead configurations in a DDD pacing mode using the optimal atrioventricular delay (AVD) and VV were identified through echo-guided optimisation. If the patient was in atrial fibrillation VVI pacing mode was used with the optimal VV identified through echo-guided optimisation. All available quadripolar LV lead configurations/vectors were tested. Quadripolar lead configurations in which capture was not possible over 5 volts at 1.2ms were excluded, as were configurations that provoked diaphragmatic stimulation. After the acquisition of vest electrograms under each configuration, the participants, with the vest still in position, underwent a thoracic computed tomographic (CT) scan to determine the precise anatomic relation between the cardiac geometry and the torso electrodes, which was used to reconstruct 1500 unipolar electrograms on the epicardial surface of the heart. Based on each data set obtained with the ECVUE, an activation map of both ventricles was generated offline by animating the activation waveform on the subject-specific CT-derived epicardial surface. Ventricular activation times were calculated from the onset of the QRS to the maximal negative slope of each electrogram and combined to construct 3D epicardial isochrone maps. (Figure 1) Specific raw data were extracted to permit the calculation of total VaT (TVaT) and $VaT_{10\text{-}90}$ which represent a complex engineering task from custom-developed MATLAB code (MathWorks, Natick, MA) previously used by the authors [6,14].

Statistical analyses

Statistical analyses were performed using PASW Statistics 21 (SPSS Inc., Chicago, IL). Changes in VaTs were compared using the Mann-Whitney U test, ANOVA and the Kruskal–Wallis Test. Any post hoc comparisons were performed using Tukey's HSD. Correlations were assessed by the Pearson correlation test. P values less than 0.05 were deemed statistically significant.

Results

The study population consisted of 19 subjects. (Table 1). Mean age was 68±13 years, 79% were ischemic and 74% had LBBB. The baseline TVaT for the entire group was 145.5ms, and VaT_{10-90} was 83.4ms. (Table 2) When comparing ischemic and non-ischemic patients, there was no significant difference in the baseline value of TVaT (146±23 vs 144±27, ms) or VaT_{10-90} (84±18 vs 82±28, ms).

Optimization of the pacing vector

TVaT and VaT_{10-90} for each pacing vector are shown in Table 3. Vectors with a high threshold and PNS were excluded. Across all patients, there was no significant difference in the average TVaT or VaT_{10-90} based on the vectors used in either true bipolar or extended bipolar configurations, suggesting that changing the site of stimulation from the quadripolar lead did not significantly affect ventricular activation time across all patients and that no particular vector was more effective in all patients. There were significant changes in activation times in individual patients depending on the LV vector. For the entire group, the optimal pacing vector (defined as the vector that produced the shortest activation time for a particular patient) significantly decreased from baseline TVaT and $VaT_{10-90,}$ by a mean of 16±29ms and 31±23ms, respectively. TVaT and VaT_{10-90} were reduced by 19±22 and 33±17ms in ischaemic subjects and by 10±40 and 28±32ms in non-ischemic patients, respectively. (Figure 2) No single pacing vector consistently produced the shortest ventricular activation time or resulted in the most substantial reduction of ventricular activation times in comparison to the baseline values across all, ischemic or non-

ischemic patients. (Table 3) Figure 3 shows TVaT and VaT_{10-90} for the individual vectors tested for ischaemic and non-ischaemic cases.

Optimal vs worst vector programming

There were marked differences between the most and least synchronous pacing vectors for the whole group (42±23ms for TVaT and 31±16ms for VaT_{10-90}) (Table 4) this represented a 28% difference in TVaT for the optimal versus the worst configuration and 37% for VaT_{10-90}. These differences were apparent in both ischemic and non-ischemic patients (43 and 28ms for TVaT and VaT_{10-90} in ischaemic, and 41 and 36ms in non-ischaemic). Figure 4 shows the difference between the most and least synchronous pacing vectors for TVaT and VaT_{10-90} in each patient. The optimal TVaT and VaT_{10-90} timings were achieved in 47% and 63% of patients, respectively, when pacing from LV vectors that are only present in a quadripolar lead and not from the standard bipolar and extended bipolar vectors that would be available in a bipolar lead. (D1_M2 and D1_RV).

Discussion

We studied the effects of different LV stimulation configurations via a quadripolar LV lead on ventricular activation times using non-invasive ECG mapping.

The findings of the current study were:

1) CRT delivered via a quadripolar lead resulted in a significant shortening of activation times compared to baseline, consistent with efficient resynchronisation.

2) No single vector was associated with more rapid ventricular activation in all subjects. However, there were significant changes in ventricular activation times depending on the vector selected.
3) There was a marked reduction in ventricular activation times between the optimal and worst vectors in both ischemic and non-ischemic patients.
4) Optimal resynchronisation was commonly achieved using non-conventional bipolar and extended bipolar configurations only available by using a quadripolar lead.

Our findings suggest that use of the optimal stimulation electrode/vector is essential to achieve optimal resynchronisation. Unfortunately, this would appear to require individual tailoring of the vector for each patient, since no single vector was most effective for shortening of ventricular activation throughout the entire group. Our findings suggest that the difference between programming an optimal and a non-optimal configuration may significantly affect the degree of resynchronisation that can be effected by a quadripolar lead, with a 28% difference in ventricular resynchronisation assessed by TVaT compared to baseline depending on the vector used and an even greater difference of 37% for $VaT_{10\text{-}90}$ a metric which reflects the bulk of ventricular activation

Comparison with previous studies

The findings of the present study are consistent with the results of recent studies[4,15] showing that more effective CRT could be achieved with quadripolar leads compared to bipolar leads. The availability of more programming options should increase the chance that a particular patient will achieve optimal resynchronisation. A notable finding of this study, in addition to the individual variation in the optimal stimulation site, is that this individual variation was seen in both ischaemic and non-ischaemic patients. This suggests that optimal vector selection is important in both non-ischemic and ischemic subjects. While this may seem intuitive in ischemic

patients, in whom stimulation from a particular vector in proximity to scar may result in ineffective CRT, the variability seen in non-ischemic patients may reflect areas of scar/slow conduction/diffuse fibrosis which may not be readily visualised with standard imaging tools.[16] In a large proportion of cases optimal resynchronization was achieved with non-standard bipolar or extended bipolar configurations highlighting the potential benefit of the additional vectors on a quadripolar lead compared to bipolar leads. The number of subjects in whom activation times were assessed is comparable to those in previous studies.[17] Calo et al found pacing configurations using the most proximal poles offered better acute haemodynamic response. [18] In keeping with this in our non-ischaemic subjects more basal vectors produced shorter timings, which is consistent with the hypothesis that more basal stimulation may provide better resynchronisation. However, this was not the case in ischaemic individuals, where stimulation from more distal vectors was associated with more rapid ventricular activation, which may be related to the presence of scar.

Clinical significance

The use of quadripolar leads has become the standard of care, since they have been shown to be superior to bipolar leads. Initially, this was related to a reduction in PNS, but more recently, mortality benefits have been demonstrated.[4,15] The presence of additional poles makes it possible to program vectors to make CRT more effective. Programming of the optimal vector/configuration may be critical in this regard. Our findings suggest that optimisation needs to be tailored to the individual patient in order to achieve the optimal resynchronisation. This would appear to be important in ischemic as well as non-ischemic patients. Programming of vectors commonly used involving the distal pacing vectors was commonly found not to be optimal in this patient group. The data presented here are from a relatively small population at a single centre, and the findings will need to be validated in a larger study. If these findings are confirmed this may have important clinical significance and would suggest that such imaging techniques could be used program the optimal pacing vector in individual patients that may improve CRT response.

Limitations

The data presented here are from a relatively small population at a single centre, and the findings will need to be validated in a larger study. Perhaps, a larger population study could show a significant difference in ventricular activation timings between vectors used in true bipolar or extended bipolar configurations enhancing the benefits of a quadripolar lead implant. Nonetheless, the sample size is similar to those in previous studies of non-invasive mapping in CRT. We did not systemically assess the presence or distribution of myocardial scar in our patients, and it is unclear whether the results regarding activation times are directly related to the presence and distribution of scar/slow conduction. This study did not consider lead placement (all leads were targeted to a lateral or postero-lateral vein) and an assessment of activation times from different coronary veins would be of interest but is beyond the scope of the current study. Short-term clinical outcomes were not assessed and, despite acute evaluation of activation times being markers of ventricular resynchronisation, does not necessarily give insight into CRT outcomes in the long term, and further studies will be required to assess whether the acute optimisation of activation translates into long-term benefits and a response to CRT.

Conclusion

Non-invasive ECM allows assessment of the effects of quadripolar programming on ventricular activation. Changes in quadripolar configurations appear to have a significant impact in both ischemic and non-ischemic patients, and thus individual tailoring may be required to give the best response to treatment.

Funding

This work was partly supported by the NIHR Biomedical Research Centre at Guy's and St Thomas' NHS Foundation Trust and King's College London.

References

[1] Auricchio A, Prinzen FW. Non-Responders to Cardiac Resynchronization Therapy. Circ J 2011;75:521–7. doi:10.1253/circj.CJ-10-1268.

[2] Sperzel J, Danschel W, Gutleben K-J, Kranig W, Mortensen P, Connelly D, et al. First prospective, multi-centre clinical experience with a novel left ventricular quadripolar lead. Europace 2012;14:365–72. doi:10.1093/europace/eur322.

[3] Shetty AK, Sohal M, Chen Z, Ginks MR, Bostock J, Amraoui S, et al. A comparison of left ventricular endocardial, multisite, and multipolar epicardial cardiac resynchronization: an acute haemodynamic and electroanatomical study. EP Eur 2014;16:873–9. doi:10.1093/europace/eut420.

[4] Behar JM, Bostock J, Zhu Li AP, Chin HMS, Jubb S, Lent E, et al. Cardiac resynchronization therapy delivered via a multipolar left ventricular lead is associated with reduced mortality and elimination of phrenic nerve stimulation: Long-term follow-up from a multicenter registry. J Cardiovasc Electrophysiol 2015;26:540–6. doi:10.1111/jce.12625.

[5] Behar J, Toth D, Remil S, Panayiotou M, Claridge S, Jackson T, et al. 19-05: The clinical utility of real time, X-MRI guided left ventricular lead implantation for delivery of cardiac resynchronisation therapy. EP Eur 2016;18:i165–i165. doi:10.1093/europace/18.suppl_1.i165b.

[6] Sohal M, Shetty A, Niederer S, Lee A, Chen Z, Jackson T, et al. Mechanistic insights into the benefits of multisite pacing in cardiac resynchronization therapy: The importance of electrical substrate and rate of left ventricular activation. Hear Rhythm 2015;12:2449–57. doi:10.1016/j.hrthm.2015.07.012.

[7] Strik M, Van Middendorp LB, Houthuizen P, Ploux S, Van Hunnik A, Kuiper M, et al.

Interplay of electrical wavefronts as determinant of the response to cardiac resynchronization therapy in dyssynchronous canine hearts. Circ Arrhythmia Electrophysiol 2013;6:924–31. doi:10.1161/CIRCEP.113.000753.

[8] Ramanathan C, Jia P, Ghanem R, Ryu K, Rudy Y. Activation and repolarization of the normal human heart under complete physiological conditions. Proc Natl Acad Sci U S A 2006;103:6309–14. doi:10.1073/pnas.0601533103.

[9] Surawicz B, Childers R, Deal BJ, Gettes LS. AHA/ACCF/HRS Recommendations for the Standardization and Interpretation of the Electrocardiogram. Part III: Intraventricular Conduction Disturbances A Scientific Statement From the American Heart Association Electrocardiography and Arrhythmias Committee, . J Am Coll Cardiol 2009;53:976–81. doi:10.1016/j.jacc.2008.12.013.

[10] Kligfield P, Gettes LS, Bailey JJ, Childers R, Deal BJ, Hancock EW, et al. Recommendations for the standardization and interpretation of the electrocardiogram. Hear Rhythm 2007;4:394–412. doi:10.1016/j.hrthm.2007.01.027.

[11] Jones S, Shun-Shin MJ, Cole GD, Sau A, March K, Williams S, et al. Applicability of the iterative technique for cardiac resynchronization therapy optimization: full-disclosure, 50-sequential-patient dataset of transmitral Doppler traces, with implications for future research design and guidelines n.d. doi:10.1093/europace/eut257.

[12] Thomas DE, Yousef ZR, Fraser AG. A critical comparison of echocardiographic measurements used for optimizing cardiac resynchronization therapy: Stroke distance is best. Eur J Heart Fail 2009;11:779–88. doi:10.1093/eurjhf/hfp086.

[13] Cakulev I, Sahadevan J, Arruda M, Goldstein RN, Hong M, Intini A, et al. Confirmation of novel noninvasive high-density electrocardiographic mapping

with electrophysiology study: Implications for therapy. Circ Arrhythmia Electrophysiol 2013;6:68–75. doi:10.1161/CIRCEP.112.975813.

[14] Niederer SA, Shetty AK, Plank G, Bostock J, Razavi R, Smith NP, et al. Biophysical modeling to simulate the response to multisite left ventricular stimulation using a quadripolar pacing lead. PACE - Pacing Clin Electrophysiol 2012;35:204–14. doi:10.1111/j.1540-8159.2011.03243.x.

[15] Leyva F, Zegard A, Qiu T, Acquaye E, Ferrante G, Walton J, et al. Cardiac Resynchronization Therapy Using Quadripolar Versus Non-Quadripolar Left Ventricular Leads Programmed to Biventricular Pacing With Single-Site Left Ventricular Pacing: Impact on Survival and Heart Failure Hospitalization. J Am Heart Assoc 2017;6:e007026. doi:10.1161/JAHA.117.007026.

[16] Ginks MR, Lambiase PD, Duckett SG, Bostock J, Chinchapatnam P, Rhode K, et al. A simultaneous X-Ray/MRI and noncontact mapping study of the acute hemodynamic effect of left ventricular endocardial and epicardial cardiac resynchronization therapy in humans. Circ Heart Fail 2011;4:170–9. doi:10.1161/CIRCHEARTFAILURE.110.958124.

[17] Ploux S, Lumens J, Whinnett Z, Montaudon M, Strom M, Ramanathan C, et al. Noninvasive Electrocardiographic Mapping to Improve Patient Selection for Cardiac Resynchronization Therapy Beyond QRS Duration and Left Bundle Branch Block Morphology. J Am Coll Cardiol 2013;61:2435–43. doi:10.1016/j.jacc.2013.01.093.

[18] Calò L, Martino A, de Ruvo E, Minati M, Fratini S, Rebecchi M, et al. Acute echocardiographic optimization of multiple stimulation configurations of cardiac resynchronization therapy through quadripolar left ventricular pacing: A tailored approach. Am Heart J 2014;167:546–54. doi:10.1016/j.ahj.2013.12.028.

Figure 1 – Example of 3D epicardial isochrone maps obtained for Patient 4 with the LV lead configurations in a DDD pacing mode using the optimal atrioventricular delay (AVD) and VV were identified through echo-guided optimisation. A - D1 – Distal pole of an LV quadripolar lead to RV; B - M2 – 2nd Middle pole of an LV quadripolar lead to RV; C - M3 – 3rd Middle pole of an LV quadripolar lead to RV; D - P4 – Proximal pole of an LV quadripolar lead to RV; RV – Proximal pole (Coil) of an RV bipolar lead

Figure 2 – Differences in $VaT_{10\text{-}90}$ between baseline and the optimal vector in individual ischaemic and non-ischaemic subjects.

X-axes show patient identifiers.

Figure 3 - $VaT_{10\text{-}90}$ and TVaT values in individual ischaemic and non-ischaemic patients according to the LV configuration

Figure 4 – Difference between the most and least synchronous pacing vectors for $VaT_{10\text{-}90}$ and TVaT according to the LV configuration

Table 1 Subject Characteristics

	value (%)
Age (y)	68± 13
Sex	
Male	15 (79)
Female	4 (21)
Aetiology	
Ischaemic	12 (63)
Non-ischaemic	7 (37)
QRS duration (ms)	
120 – 150 ms	5 (26)
>150 ms	14 (74)
QRS morphology	
LBBB	14 (74)
Non - LBBB	5 (26)
Atrial Status	
Atrial Fibrillation	5 (26)
Sinus Rhythm	14 (74)
NHYA	
II	2 (11)
III	17 (89)

LBBB, left bundle branch block; LV, left ventricle; NYHA, New York Heart Association; Non-LBBB, non-left bundle branch block; RV, right ventricle

Table 2 Baseline Ventricular Activation Times According to Aetiology

Aetiology	N	VaT_{10-90} (ms)	TVaT (ms)
Ischaemic	12	84±18	146±23
Non-Ischaemic	7	82±28	144±27
Total	19	83.6±21	145.5±24

TVaT, total ventricular activation time; VaT_{10-90}, delay between the 10^{th} and 90^{th} percentiles of VaT

Table 3. Ventricular Activation Times under Different LV Configurations with a Quadripolar LV Lead with regard to the Aetiology

	Aetiology								
	Ischaemic			Non-Ischaemic			Total		
LV Configuration	N	VaT_{10-90} (ms)	TVaT (ms)	N	VaT_{10-90} (ms)	TVaT (ms)	N	VaT_{10-90} (ms)	TVaT (ms)
D1_RV	12	65±27	147±37	7	66±20	138±35	19	65±24	143±34
M2_RV	12	64±15	145±27	7	67±16	146±32	19	65±15	146±28
M3_RV	11	63±20	142±28	7	64±14	143±32	18	63±18	142±29
P4_RV	12	63±18	150±24	6	74±26	146±26	18	66±21	149±24
D1_P4	12	67±15	142±28	6	67±19	143±36	18	67±16	143±30
D1_M2	10	60±16	135±32	7	76±29	160±48	17	67±23	145±40
M3_M2	8	75±16	149±27	6	66±18	134±26	14	71±17	143±27
M3_P4	10	64±16	144±37	7	67±14	151±28	17	65±15	147±33
Total	87	65±18	145±29	53	68±19	145±32	140	66±19	145±30
		0.728*†	0.947*†		0.990*†	0.964*†		0.940*†	0.988*†

D1 – Distal pole of an LV quadripolar lead; M2 – 2nd Middle pole of an LV quadripolar lead; M3 – 3rd Middle pole of an LV quadripolar lead; P4 – Proximal pole of an LV quadripolar lead; RV – Proximal pole (Coil) of an RV bipolar lead

*ANOVA and Kruskal–Wallis Test within LV Configurations

†All between-group comparisons were not significant (Tukey HSD).

Only vectors with confirmed myocardial capture and the absence of PNS were used.

Table 4. Difference in VaT_{10-90} and TVaT Between the Most and Least Synchronous Pacing Vectors with Regard to Aetiology

Aetiology	N	VaT_{10-90} Worst – Optimal (ms)	TVaT Worst – Optimal (ms)
Ischaemic	12	28±12	43±23
Non-Ischaemic	7	36±21	41±25
		0.482*	0.902*
Total	19	31±16	42±23
		0.456*	0.456*

*Independent samples Kruskal-Wallis test

Highlights

- Electrical resynchronisation by VaT_{10-90} reflecting the bulk of myocardial activation
- Significant shortening compared to baseline via quadripolar lead
- Reduction between optimal and worst vectors in both ischemic and non-ischemic
- Optimal resynchronisation achieved using non-conventional bipolar configurations

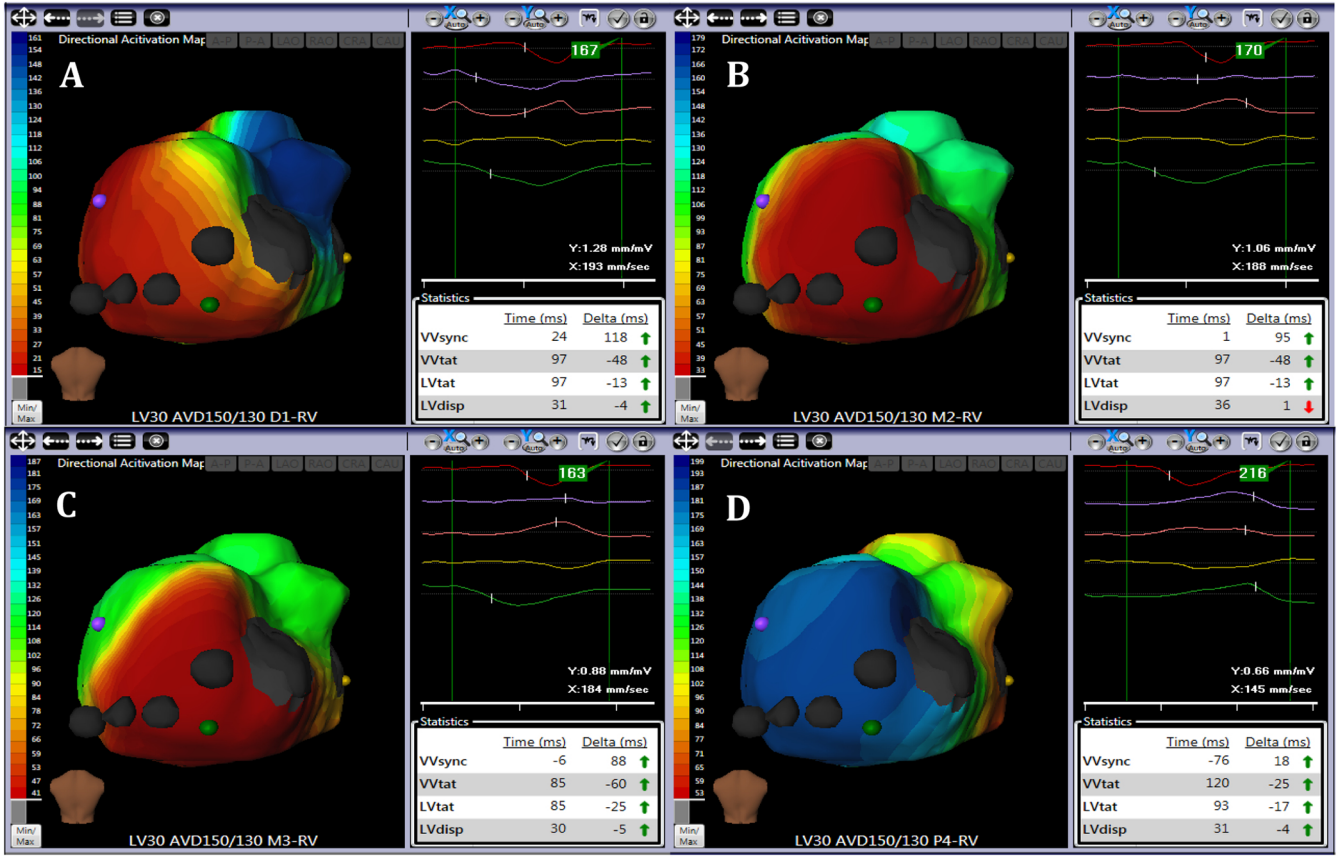
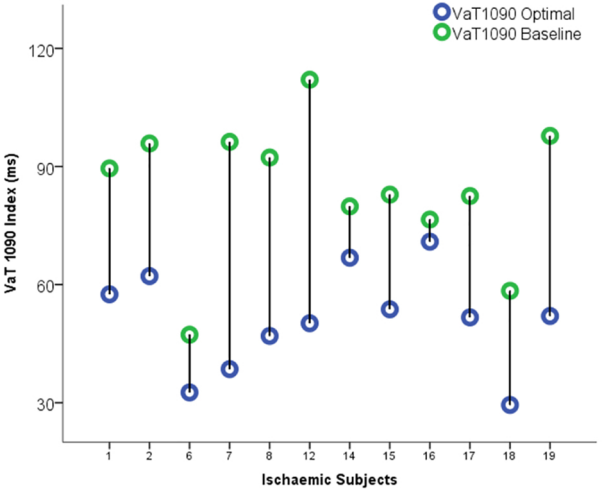

A
Directional Acitivation Map
LV30 AVD150/130 D1-RV
167
Y:1.28 mm/mV
X:193 mm/sec
Statistics
Time (ms) Delta (ms)
VVsync 24 118
VVtat 97 -48
LVtat 97 -13
LVdisp 31 -4
B
Directional Acitivation Map
LV30 AVD150/130 M2-RV
170
Y:1.06 mm/mV
X:188 mm/sec
Statistics
Time (ms) Delta (ms)
VVsync 1 95
VVtat 97 -48
LVtat 97 -13
LVdisp 36 1
C
Directional Acitivation Map
LV30 AVD150/130 M3-RV
163
Y:0.88 mm/mV
X:184 mm/sec
Statistics
Time (ms) Delta (ms)
VVsync -6 88
VVtat 85 -60
LVtat 85 -25
LVdisp 30 -5
D
Directional Acitivation Map
LV30 AVD150/130 P4-RV
216
Y:0.66 mm/mV
X:145 mm/sec
Statistics
Time (ms) Delta (ms)
VVsync -76 18
VVtat 120 -25
LVtat 93 -17
LVdisp 31 -4

Figure 1


VaT1090 Optimal
VaT1090 Baseline
VaT 1090 Index (ms)
120
90
60
30
1
2
6
7
8
12
14
15
16
17
18
19
Ischaemic Subjects

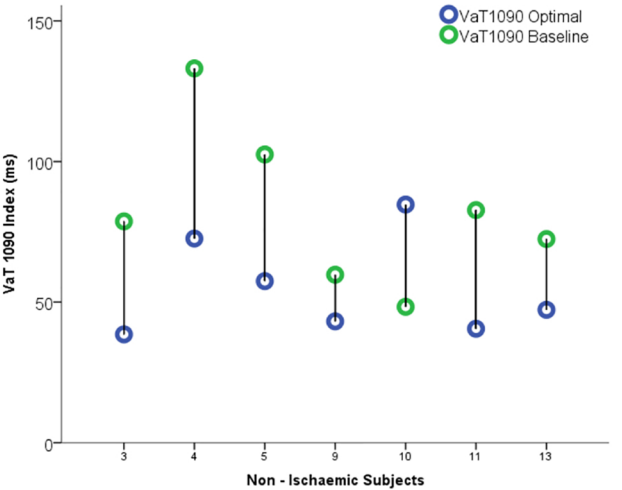
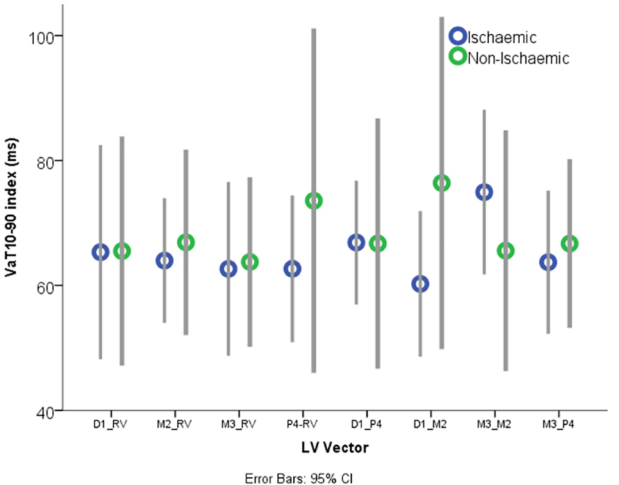

VaT1090 Optimal
VaT1090 Baseline
VaT 1090 Index (ms)
150
100
50
0
3
4
5
9
10
11
13
Non - Ischaemic Subjects

Figure 2


Ischaemic
Non-Ischaemic
VaT10-90 index (ms)
100
80
60
40
D1_RV
M2_RV
M3_RV
P4-RV
D1_P4
D1_M2
M3_M2
M3_P4
LV Vector
Error Bars: 95% CI

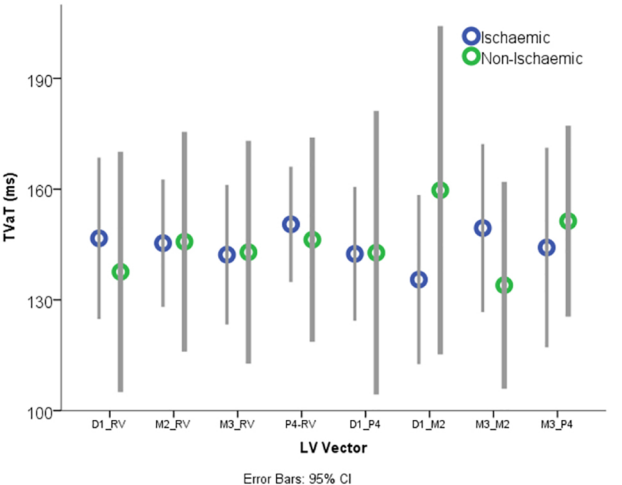
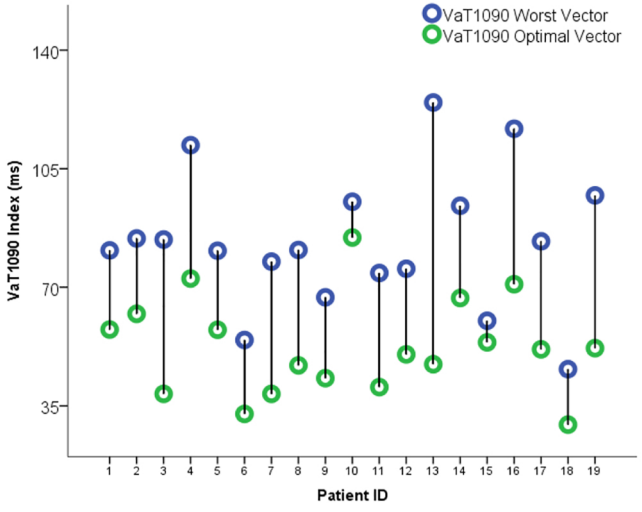

Ischaemic
Non-Ischaemic
TVaT (ms)
190
160
130
100
D1_RV
M2_RV
M3_RV
P4-RV
D1_P4
D1_M2
M3_M2
M3_P4
LV Vector
Error Bars: 95% CI

Figure 3


VaT1090 Worst Vector
VaT1090 Optimal Vector
VaT1090 Index (ms)
140
105
70
35
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
Patient ID

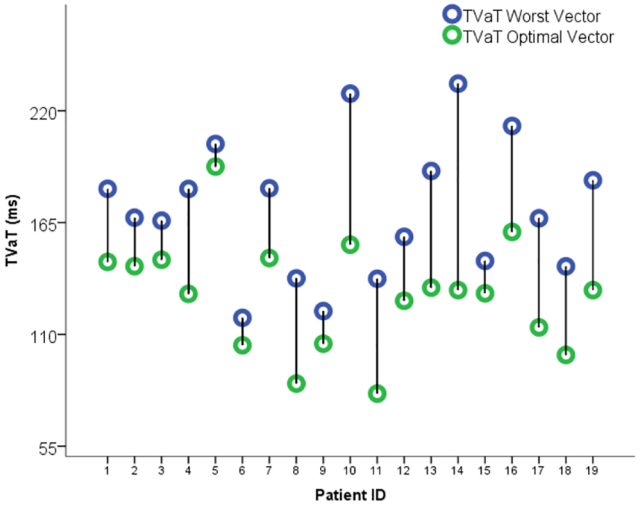

TVaT Worst Vector
TVaT Optimal Vector
TVaT (ms)
220
165
110
55
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
Patient ID

Figure 4